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| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR           | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|--------------------------------|---------------------|------------------|
| 10/740,264  | 12/17/2003  | Maria Dolores Fernandez Forner | 251502007410        | 1918             |
| 25226   | 7590        | 07/22/2004                     | EXAMINER            |                  |
| MORRISON & FOERSTER LLP<br>755 PAGE MILL RD<br>PALO ALTO, CA 94304-1018 |             |                                | AULAKH, CHARANJIT   |                  |
|   |             |                                | ART UNIT            | PAPER NUMBER     |

1625

DATE MAILED: 07/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/740,264

Applicant(s)

FERNANDEZ FORNER ET AL.

Examiner

Charanjit S. Aulakh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 24 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 36-63 is/are pending in the application.
- 4a) Of the above claim(s) 58-60 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 36,37,53,55-57 and 62 is/are rejected.
- 7) ☒ Claim(s) 38-52,54,61 and 63 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 10/047,464.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 4.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. According to paper filed on May 24, 2004, the applicants have elected group I (claims 36-55 and 61-63) with traverse in response to restriction requirement. Applicant's arguments regarding existence of unity between groups I and II according to PCT rules were persuasive. Therefore, claims 56 and 57 directed to group II have now been included in group I. However, compounds of group III do not have same core and therefore, unity of invention is lacking between new group I ( claims 36-57 and 61-63 ) and group III ( claims 58-60 ). Thus, restriction requirement is made final between new group I and group III.

2. Claims 36-63 are pending in the application. Claims 58-60 are withdrawn from further consideration as directed to non-elected group.

### ***Specification***

3. The abstract of the disclosure is objected to because it is too long. Correction is required. See MPEP § 608.01(b).

### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 62 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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The following eight different factors (see *Ex parte Foreman*, 230 USPQ at 547; *Wands, In re*, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on at least four of the above mentioned eight factors such as quantity of experimentation necessary, the amount of direction or guidance provided, the state of the prior art, presence of working examples and the breadth of claims.

The instant compounds have binding affinity for muscarinic M3 receptors and furthermore, inhibit bronchospasm response to acetylcholine in guinea pigs. The binding affinity data observed in vitro assay does not identify whether the compounds are agonists or antagonists at M3 receptors. Based on inhibition of bronchospasm response to acetylcholine, it appears that the instant compounds are antagonists at M3 receptors. However, there is no teaching either in the specification or prior art reference showing that M3 receptor antagonists are involved in the etiology of every possible known respiratory disease, gastrointestinal disease or urinary disease. There is no guidance present to show how the instant compounds having affinity for M3 receptors in vitro assay will have utility in treating every possible known respiratory, urinary and gastrointestinal disease. There are no working examples present showing efficacy of instant compounds in known animal models of every possible respiratory, urinary and

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gastrointestinal disease following their in vivo administration. The instant compounds of formula (I) encompasses hundreds of thousands of compounds based on the values of variables ©, R1-R3, n, m, p and B and therefore, in absence of such teachings, guidance and presence of working examples, it would require undue experimentation to demonstrate the efficacy of instant compounds in known animal models of every possible respiratory, urinary and gastrointestinal disease following their in vivo administration and hence their utility in treating these disease conditions.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 36, 37, 53, 55, 57 and 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 36, for the value of variables, R1-R3, the term----for example , with a hydroxy or alkoxy group ----- is vague and indefinite since it is not clear whether the alkyl groups are substituted with only these two groups or are there additional substituents also?

Claim 37 recites the limitation "R11" in claim 36. There is insufficient antecedent basis for this limitation in the claim.

In claim 53, the term --characterised in that --- is vague. The applicants are suggested to use the term ---wherein ----. Also, the IC50 values are obtained in vivo or in vitro assay? What is meant by (Hm3)? The applicants are suggested to delete this claim since it is directed to mechanism only and not any utility.

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In claim 55, the term --characterised in that --- is vague. The applicants are suggested to use the term ---wherein ----.

Claim 55 recites the limitation "the resulting reaction mixture" in claim 54. There is insufficient antecedent basis for this limitation in the claim.

Claim 57 recites the limitation "2,2,difuran for variable B (last compound)" in claim 56.

There is insufficient antecedent basis for this limitation in the claim.

In claim 62, the terms ---respiratory disease, urinary disease and/or gastrointestinal disease --- are indefinite since specific disease conditions are not defined.

### ***Claim Rejections - 35 USC § 102***

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 56 and 57 are rejected under 35 U.S.C. 102(a) as being anticipated by Gao ( Chemical J. of Chinese universities ).

Gao discloses stereochemistry of the heterocyclic alcohols containing piperidine unit.

The compounds disclosed in table 1 ( FLU, XAN, THI, Oxepin and Thiepin where R4 represents quinuclidine anticipates the instant claims when R10 represents a hydroxy group In variable B in the instant compounds of formula (III).

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 56 and 57 are rejected under 35 U.S.C. 102(b) as being anticipated by Noronha-Blob ( Eur. J. Pharmacol. ).

Noronha-Blob discloses stereoselective antimuscarinic effects of 3-quinuclidinyl atrolactate and 3-quinuclidinyl xanthene-9-carboxylate. The compound ( R )-QNX ( see table 1 on page 100 as well as fig. 1 on page 98 ) anticipates the instant claims when

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R10 represents H and Q represents O in variable B in the instant compounds of formula (III).

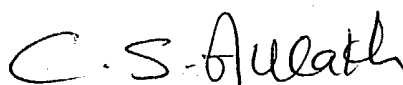
***Allowable Subject Matter***

10. Claims 38-52, 54, 61 and 63 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Charanjit S. Aulakh  
Primary Examiner  
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